

**23.** The method of claim **22**, wherein the PARP inhibitor is olaparib.

**24.** The method of claim **20**, wherein the Chk1 inhibitor is MK8776 (SCH900776), LY2603618, CCT245737, or GDC-0575.

**25.** The method of claim **20**, wherein chlorambucil is administered to the mammalian subject.

**26.** The method of claim **1**, wherein the cancer is a gastric cancer, hepatocellular carcinoma, renal cell carcinoma, esophageal cancer, pancreatic cancer, ovarian cancer, bladder cancer, lung cancer, colorectal cancer, melanoma, breast cancer, Merkel cell carcinoma, cervical cancer, hepatocellular cancer, head and neck cancer, sarcoma, lymphoma, leukemia, urothelial cancer, myelodysplasia, or sarcoma.

**27.** The method of claim **26**, wherein the cancer is an ovarian cancer, a bladder cancer, a breast cancer, or a melanoma.

**28.** The method of claim **27**, wherein the cancer is a breast cancer.

**29.** The method of claim **28**, wherein the breast cancer comprises a mutation in BRCA1.

**30.** The method of claim **28**, wherein the breast cancer does not comprise a mutation in BRCA2.

**31.** The method of claim **28**, wherein the breast cancer does not comprise a mutation in BRCA1 or BRCA2.

**32.** The method of claim **1**, wherein the cytoplasmic PD-L1 is located within the nucleus.

**33.** The method of claim **1**, wherein the measuring comprises immunohistochemistry, mass spectroscopy, immunoprecipitation, flow cytometry, or digital imaging.

**34.** The method of claim **1**, wherein the mammalian subject is a human.

**35.** The method of claim **1**, wherein the method further comprises detecting a mTORC1 signal or the one or more Lamtor proteins in the cancer.

**36.** The method of claim **35**, wherein the one or more LAMTOR protein is LAMTOR1, LAMTOR2, LAMTOR3, LAMTOR4, or LAMTOR5.

**37.** The method of claim **1**, wherein the anti-cancer therapy is an immune checkpoint blockade therapy.

**38.** The method of claim **37**, wherein the immune checkpoint blockade therapy is an antibody that selectively binds PD-1 or PD-L1.

**39.** The method of claim **1**, wherein the anti-cancer therapy is a chemotherapeutic, an immunotherapy, a gene therapy, a radiotherapy, a small molecule, a DNA therapy, an RNA therapy, a cryotherapy, a cellular therapy, a toll-like receptor agonist, a dual-targeting agent, a triple-targeting agent, or a surgery.

**40.** The method of claim **39**, wherein the anti-cancer therapy is cyclophosphamide or bevacizumab.

**41.** The method of claim **1**, wherein the cancer is a bladder cancer, a breast cancer, or a melanoma; and wherein the DDR inhibitor is a Chk1 inhibitor (Chk1i) or a PARP inhibitor (PARPi).

**42.** The method of claim **1**, wherein the cancer is a melanoma or an ovarian cancer; and wherein the anti-cancer therapy is pembrolizumab, bevacizumab, or cyclophosphamide.

**43.** The method of claim **1**, wherein the method does not comprise measuring surface PD-L1 expression by the cancer.

**44.** The method of claim **1**, wherein the method comprises measuring surface PD-L1 expression by the cancer.

**45.** The method of claim **1**, wherein the increased expression of cytoplasmic or intracellular PD-L1 indicates that greater than 50% of the total expressed PD-L1 in the cancer is cytoplasmic or intracellular PD-L1.

**46.** The method of claim **45**, wherein the increased expression has a ratio of cytoplasmic or intracellular PD-L1: surface PD-L1 of at least 1.5, or wherein the cancer expresses at least 1.5 times more cytoplasmic or intracellular PD-L1 than surface PD-L1.

**47-48.** (canceled)

**49.** The method of claim **45**, wherein the increased expression has a ratio of cytoplasmic or intracellular PD-L1: surface PD-L1 of at least 3, or wherein the cancer expresses at least 3 times more cytoplasmic or intracellular PD-L1 than surface PD-L1.

**50.** (canceled)

**51.** A method for identifying an anti-cancer compound, comprising:

- i) contacting a cancerous cell with a test compound; and subsequently
- ii) measuring the level of expression in the cancerous cell of:
  - (a) cytoplasmic PD-L1 and/or
  - (b) one or more LAMTOR proteins;

wherein the cancerous cell expresses cytoplasmic or intracellular PD-L1 and/or one or more LAMTOR proteins; and wherein a decrease in cytoplasmic or intracellular PD-L1 or one or more LAMTOR proteins in the cancerous cell indicates that the test compound has anti-cancer properties.

**52-54.** (canceled)

**55.** An in vitro method for diagnosing a cancer, comprising:

- i) obtaining a tissue sample comprising a cancer; and
- ii) measuring the level of expression in the cancer of
  - (a) cytoplasmic or intracellular PD-L1 and/or
  - (b) one or more LAMTOR proteins;

wherein if the expression of cytoplasmic or intracellular PD-L1 or one or more LAMTOR proteins is decreased relative to a normal control, then the method comprises administering an anti-cancer therapy to the subject.

**56-89.** (canceled)

**90.** A method of treating a cancer in a mammalian subject, comprising administering to the subject a therapeutically relevant dose of:

- (i) 9-(2-phosphonylmethoxyethyl)guanine (PMEG), chlorambucil, or a beta-lactam antibiotic, and
- (ii) an antibody that selectively binds PD-L1 or PD-1

to the mammalian subject, and wherein the cancer is melanoma, ovarian cancer, gastric cancer, hepatocellular carcinoma, renal cell carcinoma, esophageal cancer, pancreatic cancer, ovarian cancer, bladder cancer, lung cancer, colorectal cancer, melanoma, breast cancer, cervical cancer, hepatocellular cancer, head and neck cancer, sarcoma, lymphoma, leukemia, urothelial cancer, or myelodysplasia or sarcoma.

**91-103.** (canceled)

\* \* \* \* \*